

Amendments to the Claims

Please amend Claims 4, 5, 8, 11, 14, 17, 18, 21, 22 and 26. Please add new Claims 28-34. The Claim Listing below will replace all prior versions of the claims in the application:

Claim Listing

1. (original): A method of promoting healing of a chronic dermal skin ulcer on a subject, said method comprising the step of contacting the chronic dermal skin ulcer with an effective amount of an agonist of the non-proteolytically activated thrombin receptor, alone or in combination with an antimicrobial, a disinfectant, an antibiotic, an analgesic or an anti-inflammatory.
2. (original): The method of Claim 1 wherein the chronic dermal skin ulcer is a diabetic ulcer.
3. (original): The method of Claim 1 wherein the chronic dermal skin ulcer is a decubitus ulcer, a venous stasis ulcer or an arterial ulcer.
4. (currently amended): The method of ~~any one of Claims 1 to 3~~ Claim 1 wherein the agonist is a thrombin peptide derivative.
5. (currently amended): The method of Claim 4 wherein the agonist is a thrombin peptide derivative having the amino acid sequence R1-Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-R2 R1-Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-R2 (SEQ ID NO.: 5),
wherein:
 - R1 is -H or R3-C(O)-;
 - R2 is -OH or -NR4R5;
 - R3 is -H or a C1-C6 alkyl group; and

R4 and R5 are independently -H, a C1-C6 alkyl group or, taken together with the nitrogen atom to which they are bonded, a non-aromatic heterocyclic group; provided that zero, one, two or three amino acids at positions 1-9 and 14-23 in the thrombin peptide derivative differ from the amino acid at the corresponding position of SEQ ID NO.: 5; an *N*-terminal truncated fragment of the thrombin peptide derivative having at least fourteen amino acids; or a *C*-terminal truncated fragment of the thrombin peptide derivative having at least eighteen amino acids.

6. (original): The method of Claim 5 wherein R1 is -H and R2 is -NH2.
7. (original): The method of Claim 5 wherein R1 is -H and R2 is -OH.
8. (currently amended): The method of Claim 4 wherein the thrombin peptide derivative has the amino acid sequence R1-Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-R2 R1-Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-R2 (SEQ ID NO.: 5), provided that zero, one, two or three amino acids at positions 1-9 and 14-23 in the thrombin peptide derivative are conservative substitutions of the amino acid at the corresponding position of SEQ ID NO.: 5; an *N*-terminal truncated fragment of the thrombin peptide derivative having at least fourteen amino acids; or a *C*-terminal truncated fragment of the thrombin peptide derivative having at least eighteen amino acids.
9. (original): The method of Claim 8 wherein R1 is -H and R2 is -NH2.
10. (original): The method of Claim 8 wherein R1 is -H and R2 is -OH.
11. (currently amended): The method of Claim 8 wherein the thrombin peptide derivative has the amino acid sequence R1-Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-X1-Gly-Asp-Ser-Gly-Gly-Pro-X2-Val-R2 R1-Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-X1-Gly-Asp-Ser-Gly-Gly-Pro-X2-Val-R2 (SEQ ID NO.: 5), provided that zero, one, two or three amino acids at positions 1-9 and 14-23 in the thrombin peptide derivative are conservative substitutions of the amino acid at the corresponding position of SEQ ID NO.: 5; an *N*-terminal truncated fragment of the thrombin peptide derivative having at least fourteen amino acids; or a *C*-terminal truncated fragment of the thrombin peptide derivative having at least eighteen amino acids.

Lys-Arg-Gly-Asp-Ala- Cys-X1-Gly-Asp-Ser-Gly-Gly-Pro-X2-Val-R2 (SEQ ID NO.: 2), wherein X1 is Glu or Gln and X2 is Phe, Met, Leu, His or Val; or an *N*-terminal truncated fragment of the thrombin peptide derivative having at least fourteen amino acids; or a *C*-terminal truncated fragment of the thrombin peptide derivative having at least eighteen amino acids.

12. (original): The method of Claim 11 wherein R1 is -H and R2 is -NH2.
13. (original): The method of Claim 11 wherein R1 is -H and R2 is -OH.
14. (currently amended): The method of Claim 11 wherein the thrombin peptide derivative has the amino acid sequence R1-Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-R2 R1-Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala- Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-R2 (SEQ ID NO.: 2); an *N*-terminal truncated fragment of the thrombin peptide derivative having at least fourteen amino acids; or a *C*-terminal truncated fragment of the thrombin peptide derivative having at least eighteen amino acids.
15. (original): The method of Claim 14 wherein R1 is -H and R2 is -NH2.
16. (original): The method of Claim 14 wherein R1 is -H and R2 is -OH.
17. (currently amended): A method of Claim 4 wherein the thrombin peptide derivative has the amino acid sequence H-Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-NH2 H-Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys- Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-NH2 (SEQ ID NO.: 6).
18. (currently amended): A method of Claim 4 wherein the thrombin peptide derivative has the amino acid sequence R1-Asp-Asn-Met-Phe-Cys-Ala-Gly-Try-Lys-Pro-

Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-Met-Lys-Ser-Pro-Phe-R2 R1-Asp-Asn-Met-Phe-Cys-Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-Met-Lys-Ser-Pro-Phe-R2
(SEQ ID NO.: 3),

wherein:

R1 is -H or R3-C(O)-;

R2 is -OH or -NR4R5;

R3 is -H or a C1-C6 alkyl group; and

R4 and R5 are independently -H, a C1-C6 alkyl group or, taken together with the nitrogen atom to which they are bonded, a non-aromatic heterocyclic group; provided that zero, one, two or three amino acids at positions 1-14 and 19-33 of the thrombin peptide derivative differ from the amino acid at the corresponding position of SEQ ID NO.: 3; an *N*-terminal truncated fragment of the thrombin peptide derivative having at least fourteen amino acids; or a *C*-terminal truncated fragment of the thrombin peptide derivative having at least eighteen amino acids.

19. (original): The method of Claim 18 wherein R1 is -H and R2 is -NH2.
20. (original): The method of Claim 18 wherein R1 is -H and R2 is -OH.
21. (currently amended): The method of Claim 18 wherein the thrombin peptide derivative has the amino acid sequence R1-Asp-Asn-Met-Phe-Cys-Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-Met-Lys-Ser-Pro-Phe-R2 R1-Asp-Asn-Met-Phe-Cys-Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-Met-Lys-Ser-Pro-Phe-R2
(SEQ ID NO.: 3), provided that zero, one, two or three amino acids at positions 1-14 and 19-33 of the thrombin peptide derivative are conservative substitutions of the amino acid at the corresponding position of SEQ ID NO.: 3); an *N*-terminal truncated fragment of the thrombin peptide derivative having at least fourteen amino acids; or an *C*-terminal

truncated fragment of the thrombin peptide derivative having at least eighteen amino acids.

22. (currently amended): The method of Claim 18 wherein the thrombin peptide derivative has the amino acid sequence R1-Asp-Asn-Met-Phe-Cys-Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-X1-Gly-Asp-Ser-Gly-Gly-Pro-X2-Val-Met-Lys-Ser-Pro-Phe-R2 R1-Asp-Asn-Met-Phe-Cys-Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-X1-Gly-Asp-Ser-Gly-Gly-Pro-X2-Val-Met-Lys-Ser-Pro-Phe-R2 (SEQ ID NO 4), wherein X1 is Glu or Gln and X2 is Phe, Met, Leu, His or Val; an *N*-terminal truncated fragment of the thrombin peptide derivative having at least fourteen amino acids; a *C*-terminal truncated fragment of the thrombin peptide derivative having at least eighteen amino acids.
23. (original): The method of Claim 22 wherein R1 is -H and R2 is -NH2.
24. (original): The method of Claim 22 wherein R1 is -H and R2 is -OH.
25. (original): The method of Claim 22 wherein X1 is Glu and X2 is Phe.
26. (currently amended) The method of ~~any one of Claims 1 to 25~~ Claim 1 wherein the subject is a companion animal, a farm animal or a laboratory animal.
27. (original): A method of promoting healing of a chronic dermal skin ulcer on a subject, said method comprising the step of contacting the chronic dermal skin ulcer with an effective amount of an agonist of the non-proteolytically activated thrombin receptor in the absence of a protease inhibitor agent.
28. (new) The method of Claim 4 wherein the thrombin peptide derivative comprises a *C*-terminal amide.

29. (new): The method of Claim 27 wherein the agonist is a thrombin peptide derivative.
30. (new): The method of Claim 29 wherein the thrombin peptide derivative comprises a C-terminal amide.
31. (new): The method of Claim 27 wherein the thrombin peptide derivative has the amino acid sequence R1-Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala- Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-R2 (SEQ ID NO.: 5), provided that zero, one, two or three amino acids at positions 1-9 and 14-23 in the thrombin peptide derivative are conservative substitutions of the amino acid at the corresponding position of SEQ ID NO.: 5; an *N*-terminal truncated fragment of the thrombin peptide derivative having at least fourteen amino acids; or a *C*-terminal truncated fragment of the thrombin peptide derivative having at least eighteen amino acids.
32. (new): The method of Claim 31 wherein R1 is -H and R2 is -NH₂.
33. (new): The method of Claim 31 wherein R1 is -H and R2 is -OH.
34. (new): A method of promoting healing of a chronic dermal skin ulcer on a subject, said method comprising the step of contacting the dermal skin ulcer with an effective amount of a thrombin peptide derivative which has the amino acid sequence H-Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys- Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-NH₂ (SEQ ID NO.: 6).